On page 17, line 16, replace the paragraph, with th f ll wing new paragraph:

A3 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-bromoindoline,

On page 17, line 18, replace the paragraph, with the following new paragraph:

A4 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-hydroxymethylindoline,

On page 17, line 20, replace the paragraph, with the following new paragraph:

A5 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-aminomethylindoline,

On page 35, beginning at line 7 replace the paragraph, with the following new paragraph:

A6 (302) 1-[1-(4-fluorophenethyl)piperidin-4-yl]-6-(4-hydroxypiperidin-1-yl)carbonylmethylindole,

On page 36, beginning at line 13 replace the paragraph, with the following new paragraph:

A7 (317) 1-[1-(4-fluorophenethyl)piperidin-4-yl]-6-(2-methoxypyridin-5-yl)carbonylindole,

On pag 39, beginning at line 1, replace the paragraph, with the following new paragraph:

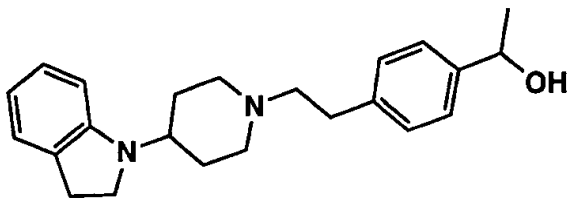
(347) 1-[1-(4-fluorophenethyl)piperidin-4-yl]-6-(1,3-dioxolan-2-yl)methylcarbamoylmethylindole,

On page 55, beginning at line 16 (bridging pages 55-56), replace the paragraph, with the following new paragraph:

Among the 1,4-substituted cyclic amine derivatives (I) according to the present invention, compounds having structures other than those as defined in the above cases (1) to (5) can be produced by the same methods as the ones as will be described in Examples hereinafter.

On page 194, beginning at line 22 (bridging pages 194-195), replace the paragraph, with the following new paragraph:

~~Example 25: Synthesis of 1-{1-[4-(1-hydroxyethyl)phenethyl]piperidin-4-yl}indoline~~

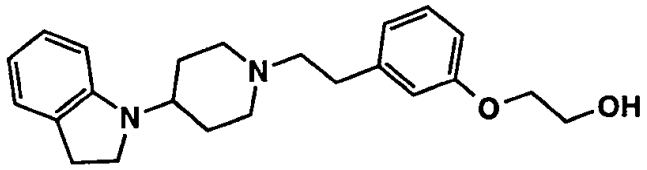


4-(1-Hydroxyethyl)phenethyl bromide (0.2 g) was treated as in Example 2 to give the title compound (0.044 g) as a yellow oil (yield: 12.6%).

On page 213, beginning at line 16 (bridging pages 213-214), replace the paragraph, with the following new paragraph:

Example 43: Synthesis of 1-{1-[3-(2-hydroxyethoxy)phenethyl]piperidin-4-yl}indoline

A11

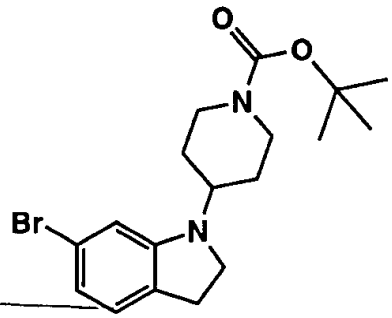


3-[2-(t-Budyldimethylsilyloxy)ethoxy]phenethyl bromide (0.33 g) was treated as in Example 24 to give the title compound (0.197 g) as a yellow oil (yield: 53.8%).

On page 274, beginning at line 4, replace the paragraph, with the following new paragraph:

Example 88: Synthesis of 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-bromoindoline

A12

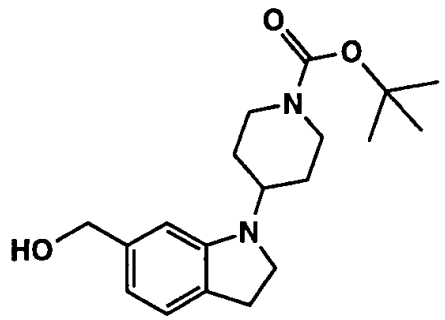


On page 274, beginning at line 8, replace the paragraph, with the following new paragraph:

Triacetoxylated sodium borohydride (11.7 g) was added to a mixture of 6-bromoindoline (8.3 g), 1-(t-butoxycarbonyl)-4-piperidone (10 g, [CAS Registry No. 7909-07-3]), acetic acid (14.9 g) and dichloroethane (200 ml) followed by stirring overnight. Then the reaction solution was concentrated under reduced pressure, and the pH value thereof was adjusted to 9 with ethyl acetate, an 8 N aqueous solution of sodium hydroxide and water and the layers were separated. The organic layer was washed with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate system) to give the title compound (10.3 g) (yield: 64%).

On page 275, beginning at line 5, replace the paragraph, with the following new paragraph:

Example 89: Synthesis of 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-hydroxymethylindoline



On page 275, b ginning at line 9 (bridging pages 275-276), replace the paragraph, with the following new paragraph:

A 2.5 M solution (16 ml) of n-butyllithium in hexane was added dropwise at -78°C into a solution of 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-bromoindoline (10 g) in tetrahydrofuran (250 ml) over 5 min. After 10 min, dimethylformamide (3.0 ml) was added and the resultant mixture was allowed to warm to room temperature. Next, a saturated aqueous solution of ammonium chloride and ethyl acetate were added thereto and the layers were separated. The organic layer was washed with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. To the residue were added ethanol (50 ml) and sodium borohydride (1.0 g) and the resultant mixture was stirred at room temperature for 30 min. Then ice water and ethyl acetate were added to the reaction solution and the layers were separated. The organic layer was washed with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate system) to give the title compound (7.9 g) (yield: 91%).

^{1}H-NMR (400 MHz, $CDCl_3$):

A15

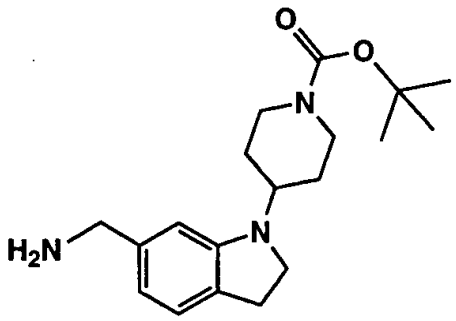
On page 276, beginning at line 11, replace the paragraph, with the f ll wing new paragraph:

Example 90: Synthesis of 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-

A16

aminomethylindoline

A16



On page 276, beginning at line 16 (bridging pages 276-277), replace the paragraph, with the following new paragraph:

Under ice cooling, a solution of diethyl azodicarboxylate (4.6 g) in tetrahydrofuran (20 ml) was added dropwise into a solution of 1-[1-(t-butoxycarbonyl)piperidin-4-yl]-6-hydroxymethylindoline (7.9 g), triphenylphosphine (6.9 g) and phthalimide (3.9 g) in tetrahydrofuran (250 ml) and the resultant mixture was stirred at room temperature for 3 hr. After concentrating under reduced pressure, the resulting residue was purified by silica gel column chromatography (ethyl acetate/hexane system). Then hydrazine hydrate (3.6 g) and ethanol (150 ml) were added thereto followed by heating under reflux for 2 hr. After ice cooling, the resulting crystalline precipitates were filtered off and the filtrate was concentrated under reduced pressure to give the title compound (8.3 g).

On page 489, beginning at lin 14 (bridging pages 489-490), replace the paragraph, with the following new paragraph:

A solution of 1-{1-[2-(4-fluorophenyl)-2-hydroxyethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline (250 mg) in methylene chloride (5 ml) was cooled to -78°C and diethylaminosulfur trifluoride (DAST, 0.1 ml) was added thereto. Then the reaction solution was stirred at the same temperature for 45 min. After the completion of the reaction, saturated sodium bicarbonate was added to the reaction solution, which was then allowed to warm to room temperature under stirring. The reaction solution was extracted with ethyl acetate and the organic layer was dried over magnesium sulfate. After evaporating the solvent, the resulting residue was purified by silica gel column chromatography (hexane/hexane system) to give 1-{1-[2-(4-fluorophenyl)-2-fluoroethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline as an oil. This product was dissolved in ethyl acetate. After adding hydrochloric acid, the resulting salt was recrystallized from ethanol/ether to give the title compound (60 mg) (yield: 24%).

m.p.: 227 - 229°C.

A18

On page 491, beginning at line 2, replace the paragraph, with the following new paragraph:

4-Bromopyridine hydrochloride 7.04g (1.0 equivalent) was partitioned between an aqueous solution of sodium hydroxide and diethyl ether. The

A19

organic layer was separated and dried over magnesium sulfate. Under nitrogen atmosphere, this solution was cooled to -78°C. Then a 1.6 M solution (25.0 ml, 1.0 equivalent) of n-butyllithium in hexane was added dropwise thereinto and the resultant mixture was stirred for additional 30 min. Next, 6-methoxytetralone (7.049 g, 4.0 mmol) dissolved in tetrahydrofuran (50 ml) was added thereto and the resultant mixture was gradually warmed to room temperature while stirring continuously. After adding a saturated aqueous solution of ammonium chloride, the mixture was extracted with ethyl acetate. The organic layer was washed with brine and dried over magnesium sulfate. After evaporating the solvent under reduced pressure, the residue was reprecipitated from chloroform/n-hexane to give the title compound (4.019 g) as a pale yellowish brown powder (yield: 39.4%).

A19

On page 537, beginning at line 4, replace the paragraph, with the following new paragraph:

Example 302: Synthesis of 1-[1-(4-fluorophenethyl)piperidin-4-yl]-6-(4-hydroxypiperidin-1-yl)carbonylmethylindole

A20

On page 559, beginning at line 12, replace the paragraph, with the following new paragraph:

A21

Example 317: Synthesis of 1-[1-(4-fluorophenethyl)piperidin-4-yl]-6-(2-methoxypyridin-5-yl)carbonylindole

On page 595, beginning at line 23, replace the paragraph, with the following new paragraph:

A22

~~Example 347: Synthesis of 1-[1-(4-fluorophenethyl)piperidin-4-yl]-6-(1,3-dioxolan-2-yl)methylcarbamoylmethylindole~~methylindole

On page 598, beginning at line 4, replace the paragraph, with the following new paragraph:

A23

Triacetoxylated sodium borohydride (15.0 g) was added under ice cooling to a liquid mixture of 6-bromoindoline (9.0 g), 1-(2-fluorophenethyl)piperidin-4-one (11.0 g) and acetic acid (12.5 ml) in 1,2-dichloroethane (140 ml). Then the reaction mixtures were stirred at room temperature overnight. The reaction mixtures were diluted with ethyl acetate (400 ml) and then an 8 N aqueous solution (70 ml) of sodium hydroxide was added thereto. The organic layer was separated, extracted with 5 N hydrochloric acid (100 ml) and then basified with an 8 N aqueous solution of sodium hydroxide. Then it was extracted with ethyl acetate and washed successively with water and brine. The ethyl acetate layer was dried over magnesium sulfate and the solvent was evaporated distilled off under reduced pressure to give the title compound (12.2 g) as a pale yellow solid (yield: 66.6 %).